Paper No. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte HELGE LUBENOW, KERSTIN STEINERT, ROLAND FABIS, JOACHIM RIBBE and MELANIE EMMERLICH

Appeal No. 2002-1292
Application No. 09/353,407[1]

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER and GREEN, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the final rejection of claims 1-50 and 52-66.[2]

Claims 1 and 2 are representative of the subject matter on appeal and read as follows:

1. A method of separating particles from a solution while minimizing particle loss comprising the steps of:
(a) combining a solution and a finely divided particulate matrix material, where said matrix material is insoluble in said solution, in the presence of a detergent;
(b) collecting the particles of the particulate matrix material; and
(c) separating the supernatant from the particulate matrix material.

[1] Application for patent filed July 15, 1999.

[2] According to the examiner, claims 1-66 stand finally rejected (Answer, page 3), but claim 51 is not included in any rejection in either the final office action or the Answer.

2. In a method for isolating a molecule from a sample in a vessel using affinity particles, comprising the steps of:

(a) combining the sample containing a molecule of interest with affinity particles suitable for binding said molecule, said affinity particles being insoluble in the sample;

(b) collecting the affinity particles;

(c) separating the affinity particles from the unbound remainder of the sample;

(d) optionally, resuspending the affinity particles in a solution;

(e) optionally, eluting said molecule from the affinity particles, followed by separating the affinity particles from said eluted molecule;

the improvement wherein at least one of steps (a), (b), (c), (d) if present, and (e) if present is performed in the presence of detergent wherein the amount of detergent is sufficient to reduce loss of particles during any separation step, in comparison to the same method performed in the absence of detergent.

The references relied on by the examiner are:

Stein et al. (Stein)	4,009,213	Feb. 22, 1977
Weisburg	5,466,577	Nov. 14, 1995
McCoy et al. (McCoy)	5,646,016	Jul. 8, 1997
Gallant et al. (Gallant)	7,798,442	Aug. 25, 1998
Zhang et al. (Zhang)	5,942,391	Aug. 24, 1999

The claims stand rejected as follows:

I. Claims 1-4, 9, 13-19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 under 35 U.S.C. § 102(e) as anticipated by Zhang.

II. Claims 1-19, 23, 24, 31-50, 54, 55 and 62-66 under 35 U.S.C. § 103 as unpatentable over Zhang and McCoy.

III. Claims 1-4, 9, 13-19, 21, 23, 29-35, 44-50, 52, 54, 55 and 60-66 under 35 U.S.C. § 103 as unpatentable over Zhang and Gallant.

IV. Claims 1-4, 9, 13-19, 22, 27-29, 31-35, 44-50, 52-55 and 58-66 under 35 U.S.C. § 103 as unpatentable over Zhang and Stein.

V. Claims 1-4, 9, 13-17, 20, 33-35, 44-46, 48, 49 and 64-66 under 35 U.S.C. § 102(b) as anticipated by Weisburg.

VI. Claims 1-4, 9, 13-17, 20, 25, 26, 33-35, 44-49, 56, 57 and 64-66 under 35 U.S.C. § 103 as unpatentable over Weisburg.

On consideration of the record, we affirm rejections I through IV, but reverse rejections V and VI.

BACKGROUND

> Affinity separation techniques are increasingly used for the isolation or quantification of biological molecules. Chromatographic techniques that use magnetically attractable affinity particles or beads for separation of specific molecules from a liquid are well documented in biochemical, biomedical, and molecular biological research. Affinity separation techniques involve the suspension of finely divided affinity matrix particles in a solution that contains molecules of interest in an impure or dilute form. The molecules of interest are captured or immobilized on the matrix particles by virtue of specific or non-specific interactions between the molecules and an affinity ligand or such molecules associated with the surface of the affinity particles. The affinity particles and the bound target molecules of interest may then be separated or collected together using a variety of standard techniques, such as filtration, centrifugation, decanting, and the like.
>
> Particularly useful materials and techniques . . . utilize magnetically attractable affinity beads. After binding the target molecule, application of a magnetic field to the vessel containing the magnetic affinity particles (beads) will cause them to migrate towards the source of the field, thus collecting and concentrating the beads at the wall of the vessel. With the magnetic field still applied, the remainder of the solution and unbound components (the supernatant) can be removed by pouring it off or by using a pipetting device, leaving the magnetically collected pellet of magnetic particles intact. Additional solution(s) can then be added and the magnetic field removed, thus allowing the beads to be resuspended. If the interaction between the magnetic affinity beads and the molecules of interest is disrupted (target molecule eluted), the molecules can be recovered by reapplying the field and removing and retaining the supernatant containing the purified/concentrated molecules of interest . . .

Specification, pages 1-2.

> Regardless of the type of ligand used to capture the molecule of interest, affinity separation techniques suffer from a common problem of bead loss during the separation process. This problem has been observed during automated as well as manual bead handling each time the affinity beads are washed, molecules are eluted from the beads, or supernatant liquids are removed or retrieved. If the beads are collected at the bottom of a vessel, such as a microtiter plate, there is a high risk that while removing solution, some beads will also be removed. The loss or removal of beads leads to irreproducible results, inaccurate quantitation of bound materials, lower yields in purification protocols, and a lower throughput in assays.

Specification, page 3.

According to appellants, "[t]he present invention relates to methods for separating solid particles from a solution while minimizing loss of particles . . . based on the discovery that treating or exposing the beads with detergent improves the handling of the particles, and, with respect to isolation of a molecule of interest, improves the yield . . . [and] the reproducibility of the separation . . . detergent[ ] also significantly reduces loss of particles in the course of separation processes, and for affinity separations increases signal and allows for higher signal to noise ratios." Specification, page 7. "The detergents used in the methods of the present invention are nonionic, anionic, zwitterionic, and cationic detergents, and combinations thereof" and, according to the specification, the concentration of detergent effective in minimizing particle loss is "[p]referably . . . at least about 0.0005-2.0% (v/v)." Id., page 6.

GROUPING OF CLAIMS

There are six rejections of record; for convenience, we have identified them above as rejections I-VI. "[A]ll of the independent claims are subject to all of the rejections," and "[a]ppellants believe that Claims 1-66 stand or fall together" "with respect to [each of] the grounds of rejection" (Brief, page 8), except that "if . . . the Jepson format claims (Claims 2, 34, 64 and 66) are to be accorded a different scope than the other independent claims (i.e., Claims 1 and 33), . . . [then appellants] request that for each ground of rejection the Jepson format claims be considered separately from the other independent claims" (id.).

We find claim 2 (a Jepson format claim directed to an affinity particle separation method) to be narrower than claim 1 (a non-Jepson format claim directed to a particle separation method, but not necessarily involving affinity particles), but we find no

arguments directed to the separate patentability of any claim in particular, much less arguments based on this difference in scope.[3] Nevertheless, some of appellants' arguments are specific to affinity particle separation, thus, for each ground of rejection, we will consider claim 2 as representative of those rejected claims directed to affinity particle separation, and claim 1 as representative of those rejected claims that are not so limited.

DISCUSSION

With respect to all of the rejections, appellants argue essentially that the "claimed invention improves all prior art affinity procedures wherein the affinity particles are manipulated in the absence of detergent," but "none of the references relied on by the [e]xaminer, either alone or in combination, provides any substantial evidence of knowledge of the problem or how to prevent or reduce loss of affinity particles during manipulations of the particles in the absence of detergent," even though "various types of cell lysis buffers, hybridization buffers, and wash buffers with or without detergent have been developed and used . . . for decades." Brief, page 10.

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[3] "37 CFR §1.192(c)(5) [now § 1.192(c)(7)] requires the appellant to perform two affirmative acts in his brief in order to have the separate patentability of a plurality of claims subject to the same rejection considered. The appellant must (1) state that the claims do not stand or fall together and (2) present arguments why the claims subject to the same rejection are separately patentable." Ex parte Schier, 21 USPQ2d 1016, 1018 (Bd. Pat. App. Int. 1991) (emphasis in original). In the situation where (i) the appellant complies with only one of the requirements of Rule 192(c)(7), (ii) the examiner treats the claims as standing or falling together, and (iii) the appellant does not challenge that treatment of the claims, the Board "will simply decide the appeal and will decline to consider the patentability of the claims separately in reaching [its] decision." Id. at 1019.

I. Anticipation by Zhang

Claims 1-4, 9, 13-19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 stand rejected under 35 U.S.C. § 102(e) as anticipated by Zhang. Appellants concede that "[s]ome examples in Zhang" use "streptavidin-coated paramagnetic beads and a buffer, such as lysis buffer, hybridization wash buffer, or a hybridization reaction buffer, which contains a non-ionic detergent" (Brief, page 4), but argue that the reference "provides no indication of an appreciation for or a knowledge of the difference in using affinity particles that have or have not been exposed to a detergent" (id., page 10).

Appellants' arguments notwithstanding, we find no limitation in claim 2 serving to distinguish the claimed method from that described by Zhang. Claim 2, directed to a "method for isolating a molecule . . . using affinity particles," requires the presence of detergent, in an amount sufficient to reduce loss of particles during any separation step in comparison to the same method performed in the absence of detergent, in at least one of the following steps: (a) combining the sample with the affinity particles; (b) collecting the affinity particles; and (c) separating the affinity particles from unbound sample.

Zhang describes an affinity separation method wherein a detergent is present during several steps of the process: while a sample is combined with affinity particles; while the affinity particles are collected; while the affinity particles are separated from unbound sample; etc. Moreover, the amount of detergent present during the process falls within the range asserted to be effective in reducing particle loss (see page 6 of the present specification). For example, at column 27, lines 30-52, Zhang describes the capture and detection of HIV-1 RNA as follows (emphasis added):

> Target HIV-1 RNA (100 µl) is dissolved in an equal volume of lysis buffer comprising 5 M GnSCN, 100 mM EDTA, 200 mM Tris-HCl (pH 8.0), 0.5% NP-40 [ ], and 0.5 t BSA in a 1.5 ml microfuge tube. Next, the 3'-biotinylated Capture/Amp-probe-1 (HIV) [ ] and Amp-probe-2 (HIV) [ ], together with streptavidin-coated paramagnetic beads [ ] were added to the lysed sample in the lysis buffer. A complex comprising target RNA/Capture/Amp-probe-1 (HIV)/Amp-probe-2 (HIV)/paramagnetic beads was formed and retained on the beads. A magnetic field generated by a magnet in a microfuge tube holder rack [ ] was applied to the complex to retain it on the side of the reaction tube adjacent the magnet to allow unbound material to be siphoned off. The complex was then washed twice with 1.5 M GnSCN buffer to remove any unbound proteins, nucleic acids and probes [ ] trapped with the complex. The magnetic field technique facilitated the wash steps. The GnSCN was removed by washing the complex with 300 mM KCl buffer (300 mM KCl buffer, 50 mM Tris-HCl, pH 7.5, 0.5% non-IDEP-40 1 mM EDTA).

Thus, we find that Zhang describes all of the manipulative steps of claim 2. It follows that all of the manipulative steps of claim 1 are described as well (claim 1 merely requires combining a solution and a finely divided insoluble particulate matrix material in the presence of a detergent; collecting the particles of the particulate matrix material; and separating the supernatant from the particulate matrix material).

It is well established that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. See In re Woodruff, 919 F.2d 1575, 1577, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). According to appellants, "Woodruff is not applicable to the facts of Appellants' claimed methods" (page 5), because "Woodruff's disclosure actually was that the same prior art method . . . for preventing [storage and enzymatic] deterioration was also effective against one other known cause of such deterioration, i.e., fungi." Reply Brief, page 4. "In contrast," appellants argue that they "have discovered how to prevent or minimize loss of affinity

particles during manipulations . . . [by] contacting affinity particles with detergent," and "no reference . . . cited by the [e]xaminer discloses this problem either specifically or generically." Id., page 5.

We fail to see the distinction appellants do. Zhang describes a method with all of the same manipulative steps of claim 2 (and of claim 1). What appellants have discovered, and are now claiming, is not a new method, but a newly recognized benefit of an old method. Presumably, particle loss would have been greater in Zhang's affinity particle separation method, had the method been performed in the absence of detergent. In our view, Woodruff is decidedly on point, and it is of no consequence that Zhang does not discuss the effects of the detergent included in various stages of their process.

Appellants' reliance on In re Zierden, 411 F.2d 1325, 1329, 162 USPQ 102, 105 (CCPA 1969), does not persuade us otherwise. Appellants argue while "[i]t may be that some of the examples in . . . Zhang . . . may have enjoyed the benefit of practicing Appellants' claimed invention," "such a practice . . . is only an example of an accidental use, unrecognized by [ ] the cited reference[ ]," which, according to appellants' reading of Zierdan, is "without legal significance as to an anticipation." Brief, page 17. First of all, appellants appear to be referring to an argument made by the appellant in Zierden, not to any holding of the court. Indeed, in Abbott Labs. v. Geneva Pharms., Inc., 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1309 (Fed. Cir. 1999), the court reiterated that the "accidental, unintended and unappreciated production of a product or process in question" is not a bar to patentability only when the claimed invention is anticipated "by

earlier work that produced no useful or appreciated result." That is not the case here, where Zhang discloses a useful affinity particle separation method. Moreover, in Zierden, claims to a method of removing and preventing alluvium deposits in water systems - by adding to such systems insoluble potassium metaphosphate and a solubilizing agent - were found to be patentable over prior art disclosing addition of the same materials to "industrial waters" to prevent the build-up of scale, at least in part, because there was insufficient evidence to show that the water systems treated (i.e., the materials acted upon) by the claimed and prior art method were the same. Id. at 1330, 162 USPQ at 306. There is no such distinction between Zhang and the present claims.

Appellants do not deny that Zhang describes all of the manipulative steps of claim 2. On the facts presented, it appears that appellants merely claim a new benefit of an old process; the discovery that the presence of detergent in Zhang's procedures involving affinity particles confers an additional benefit (or effect) not mentioned by Zhang, i.e., that the presence of detergent minimizes particle loss during separations, cannot render the claimed process again patentable. It follows that appellants have not identified any limitation in claim 1, which is even broader than claim 2, serving to distinguish the claimed method from that described by Zhang.

On this record, appellants have not identified a limitation that serves to distinguish claim 1 or 2 over Zhang, thus, we affirm the examiner's rejection of claims 1 and 2 under 35 U.S.C. § 102(e). As previously indicated, claims 3, 4, 9, 13-19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 fall together with claims 1 and 2.

II. Zhang and McCoy; III. Zhang and Gallant; and IV. Zhang and Stein

Claims 1-19, 23, 24, 31-50, 54, 55 and 62-66 stand rejected under 35 U.S.C. § 103 as unpatentable over Zhang and McCoy (rejection I); claims 1-4, 9, 13-19, 21, 23, 29-35, 44-50, 52, 54, 55 and 60-66 stand rejected under 35 U.S.C. § 103 as unpatentable over Zhang and Gallant (rejection II); and claims 1-4, 9, 13-19, 22, 27-29, 31-35, 44-50, 52-55 and 58-66 stand rejected under 35 U.S.C. § 103 as unpatentable over Zhang and Stein (rejection IV). Again, we find no arguments directed to the separate patentability of any claim in particular, and we note appellants' "belie[f] that Claims 1-66 stand or fall together" "with respect to [each of] the grounds of rejection" (Brief, page 8). Accordingly, for each ground of rejection, we will consider claim 2 as representative of those rejected claims directed to affinity particle separation, and claim 1 as representative of those rejected claims that are not so limited.

With respect to rejections II, III and IV, appellants argue (Brief, page 14) that

> [T]here is no reference of record that either recognizes the technical problem addressed by the invention, no reference that includes a hint of a teaching relating to modification of standard affinity purification protocols, and in fact no reference that relates directly to affinity separation procedures at all. In view of this reliance on art that is not even the field of the invention, Appellants need not exhaustively analyze the combined teachings of the references. Zero + zero is still zero: that is, since there is no teaching relevant to the modification of affinity separation methods contained in any reference cited by the Examiner, any individual reference OR ANY COMBINATION of such references remains devoid of a relevant teaching.
>
> Clearly, no combination of the references cited by the Examiner is able to provide any recognition of the problem of, or Appellants' solution to, particle loss during manipulations of affinity particles in affinity separation methods.

This argument is not persuasive. As discussed above, "modification of [Zhang's] standard affinity purification protocols" to include detergent is unnecessary, as Zhang explicitly describes affinity separation of target DNA using magnetic particles in the presence of detergent, appellants' argument notwithstanding. Inasmuch as we have determined that the subject matter of claim 2, and claim 1, (which is even broader) is anticipated by Zhang, we find that the subject matter of these claims would have been prima facie obvious under 35 U.S.C. § 103 as well ("lack of novelty is the epitome of obviousness," In re May, 574 F.2d 1082, 1089, 197 USPQ 601, 607 (CCPA 1978)).

Moreover, as appellants have not presented arguments directed to the separate patentability of any claim in particular, and additionally, have indicated their belief that the claims stand or fall together with respect to each rejection, we find no error in the examiner's determination that claims 3-19, 23, 24, 31-50, 54, 55 and 62-66 would have been prima facie obvious over the combined teachings of Zhang and McCoy; claims 3, 4, 9, 13-19, 21, 23, 29-35, 44-50, 52, 54, 55 and 60-66 would have been prima facie obvious over Zhang and Gallant; and claims 3, 4, 9, 13-19, 22, 27-29, 31-35, 44-50, 52-55 and 58-66 would have been prima facie obvious over Zhang and Stein - together with claims 1 and 2.

Accordingly, we affirm rejections II, III and IV under 35 U.S.C. § 103.

V. Anticipation by Weisburg

In reviewing the portion of Weisburg relied on by the examiner (Example 3), we find insufficient evidence to establish the presence of detergent during the manipulation of a finely divided particulate matrix material as required by the claims, much less the presence of detergent in an amount asserted to be effective to reduce particle loss during manipulation. Thus, we find that the examiner has not established a prima facie case of anticipation.

Accordingly, the rejection of claims 1-4, 9, 13-17, 20, 33-35, 44-46, 48, 49 and 64-66 under 35 U.S.C. § 102(b) as anticipated by Weisburg is reversed.

VI. Obviousness over Weisburg

The examiner's rejection does not address the deficiencies of Weisburg discussed above. Accordingly, the rejection of claims 1-4, 9, 13-17, 20, 25, 26, 33-35, 44-49, 56, 57 and 64-66 under 35 U.S.C. § 103 as unpatentable over Weisburg is reversed.

CONCLUSION

We have affirmed the rejection of Claims 1-4, 9, 13-19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 under 35 U.S.C. § 102(e) as anticipated by Zhang; the rejection of claims 1-19, 23, 24, 31-50, 54, 55 and 62-66 under 35 U.S.C. § 103 as unpatentable over Zhang and McCoy; the rejection of claims 1-4, 9, 13-19, 21, 23, 29-35, 44-50, 52, 54, 55 and 60-66 under 35 U.S.C. § 103 as unpatentable over Zhang and Gallant; and the rejection of claims 1-4, 9, 13-19, 22, 27-29, 31-35, 44-50, 52-55 and 58-66 under 35 U.S.C. § 103 as unpatentable over Zhang and Stein. We have, on the other hand, reversed the rejection of claims 1-4, 9, 13-17, 20, 33-35, 44-46, 48, 49 and 64-66 under

35 U.S.C. § 102(b) as anticipated by Weisburg; and the rejection of claims 1-4, 9, 13-17, 20, 25, 26, 33-35, 44-49, 56, 57 and 64-66 under 35 U.S.C. § 103 as unpatentable over Weisburg. By our action today, claims 20, 25, 26, 56 and 57 are free of rejection (as mentioned previously, claim 51 was not the subject of this appeal, and also appears to be free of rejection).

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

William F. Smith
Administrative Patent Judge

Toni R. Scheiner
Administrative Patent Judge

Lora M. Green
Administrative Patent Judge

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